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(54) Title: DISEASE RISK ESTIMATING METHOD USING SEQUENCE POLYMORPHISMS IN A SPECIFIC REGION OF **CHROMOSOME 19**

(57) Abstract: The present invention provides methods and compositions for identifying human subjects with an increased risk of having or developing disease. In particular, this invention relates to the identification and characterization of polymorphisms in the human chromosome 19q, the region r located approximately 19q13.2-3 correlated with increased risk of developing disease, in particular cancer and the responsiveness of a subject to various treatments for cancer. An allele in the r region can be identified as correlated with an increased risk of developing disease, in particular cancer, the prognosis of developed disease, in particular cancer, and responsiveness to disease treatment, in particular cancer treatment on the basis of statistical analyses of the incidence of a particular allele in individuals diagnosed with disease, in particular cancer. The invention further relates to probes and kits comprising the probes useful in the diagnostic.





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C. DOCUM	IENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the	Relevant to daim No.		
P,X	YIN JIAOYANG ET AL: "Multiple nucleotide polymorphisms on he chromosome 19q13.2-3 associate of basal cell carcinoma." CANCER EPIDEMIOLOGY BIOMARKER: PREVENTION, vol. 11, no. 11, November 2002 pages 1449-1453, XP002261348 ISSN: 1055-9965 (ISSN print) abstract, table 1, 2 & 4; disc	1-22, 24-35,37		
X Furt	ther documents are listed in the continuation of box C.	X Patent family	members are listed in annex.	
"A" docume consider to consider the consider to consider the consideration that consider the consideration that consideration that consideration the considera	ent defining the general state of the art which is not dered to be of particular relevance document but published on an after the international date ent which may threat doubts on priority claim(s) or is cited to establish the publication date of another on or other special reason (as specified) sent referring to an oral disclosure, use, exhibition or means the published prior to the international filing date but than the priority date claimed	of priority date a cited to understa invention "X" document of particannot be constituted an invention "Y" document of particannot be constituted an invention of particannot be constituted and the constituted and the structure of the structur	ibliahed after the international filing date and not in conflict with the application but and the principle or theory underlying the cular relevance; the claimed invention dered novel or cannot be considered to the step when the document is taken alone cular relevance; the claimed invention dered to involve an inventive step when the ablaced to involve an inventive step when the ablaced with one or more other such documbination being obvious to a person skilled or of the same patent family	
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C'(C'OLITTIE	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	10.1
Category *	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to daim No.
P,X	NEXO BJORN A ET AL: "A specific haplotype of single nucleotide polymorphisms on chromosome 19q13.2-3 encompassing the gene RAI is indicative of post-menopausal breast cancer before age 55." CARCINOGENESIS (OXFORD), vol. 24, no. 5, May 2003 (2003-05), pages 899-904, XP002261349 ISSN: 0143-3334 the whole document	1-35,37
P,X	ROCKENBAUER ESZTER ET AL: "Association of chromosome 19q13.2-3 haplotypes with basal cell carcinoma: Tentative delineation of an involved region using data for single nucleotide polymorphisms in two cohorts" CARCINOGENESIS (OXFORD), vol. 23, no. 7, July 2002 (2002-07), pages 1149-1153, XP002261350 ISSN: 0143-3334 the whole document	1-35,37
P,X	YIN JIAOYANG ET AL: "Twelve single nucleotide polymorphisms on chromosome 19q13.2-13.3: Linkage disequilibria and associations with basal cell carcinoma in Danish psoriatic patients." BIOCHEMICAL GENETICS, vol. 41, no. 1-2, February 2003 (2003-02), pages 27-37, XP002261351 ISSN: 0006-2928	31-35,37
P,A	tables I,II	1-30
P,X	BERGAMASCHI DANIELE ET AL: "iASPP oncoprotein is a key inhibitor of p53 conserved from worm to human." NATURE GENETICS, vol. 33, no. 2, February 2003 (2003-02), pages 162-167, XP002272762 ISSN: 1061-4036 (ISSN print) page 163, column 2, paragraph 3 page 166, column 1, paragraph 1	36
X	SHEN M RICHARD ET AL: "Nonconservative amino acid substitution variants exist at polymorphic frequency in DNA repair genes in healthy humans" CANCER RESEARCH, vol. 58, no. 4, 15 February 1998 (1998-02-15), pages 604-608, XP002261352 ISSN: 0008-5472 table 1	31-35,37
	-/	1

Form FCT/ISA/210 (cominuation of socand sheet) (January 2004)

13

Category °	VOGEL ULLA ET AL: "Polymorphisms of the	31-35,37
X	NOGEL BILA EL AL! "POLYMOTONISMS OT THE	
	DNA repair gene XPD: Correlations with risk of basal cell carcinoma revisited" CARCINOGENESIS (OXFORD), vol. 22, no. 6, June 2001 (2001-06), pages	31-33,37
	899-904, XP002261353 ISSN: 0143-3334 page 900, column 1, paragraph 3 - paragraph 7	
Α	page 903, column 1, paragraph 4	1-35,37
X	DYBDAHL MARIANNE ET AL: "Polymorphisms in the DNA repair gene XPD: Correlations with risk and age at onset of basal cell carcinoma" CANCER EPIDEMIOLOGY BIOMARKERS AND PREVENTION, vol. 8, no. 1, January 1999 (1999-01), pages 77-81, XP002261354 ISSN: 1055-9965 page 78, column 1, paragraph 6	31-35,37
X	WO 95 16791 A (UNIV MCGILL ;POIRIER JUDES (CA)) 22 June 1995 (1995-06-22) claim 19	31-35,37
x	CHEN PENGCHIN ET AL: "Association of an ERCC1 polymorphism with adult-onset glioma" CANCER EPIDEMIOLOGY BIOMARKERS AND PREVENTION, vol. 9, no. 8, August 2000 (2000-08), pages 843-847, XP002261355 ISSN: 1055-9965	30
A	page 846, column 1, paragraph 4 abstract	1-35,37
X .	YANG JIAN-PING ET AL: "Identification of a novel inhibitor of nuclear factor-kappaB, RelA-associated inhibitor" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 22, 28 May 1999 (1999-05-28), pages 15662-15670, XP002261356 ISSN: 0021-9258 the whole document	30
A		1-35,37
X	EP 1 146 054 A (ONO PHARMACEUTICAL CO) 17 October 2001 (2001-10-17) abstract; claim 10	36
	-/	

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

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	Olion) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
Category *	Citation of document, with indication, where appropriate, or the relevant passages	· · · · · · · · · · · · · · · · · · ·		
A	BREWSTER A M ET AL: "The association between polymorphisms in the xeroderma pigmentosum group D gene and risk of breast cancer" AMERICAN JOURNAL OF EPIDEMIOLOGY, vol. 153, no. 11 Supplement, 1 June 2001 (2001-06-01), page S198 XP002261357 Joint Meeting of the Society for Epidemiologic Research, American College of Epidemiology, Epidemiol; Toronto, Canada; June 13-16, 2001 ISSN: 0002-9262 the whole document	1-35,37		
A	BUTKIEWICZ DOROTA ET AL: "Genetic polymorphisms in DNA repair genes and risk of lung cancer" CARCINOGENESIS (OXFORD), vol. 22, no. 4, April 2001 (2001-04), pages 593-597, XP002261358 ISSN: 0143-3334 abstract; table II; discussion	1-35,37		

3

ation on patent family members

PC170K 03/00448

E .	Palent document ed in search report		Publication date		Patent family member(s)	Publication date
W	0 9516791	Α	22-06-1995	CA AU WO	2111503 A1 1189395 A 9516791 A1	16-06-1995 03-07-1995 22-06-1995
E	P 1146054	Α	17-10-2001	EP US WO JP US	1146054 A1 6582933 B1 0032628 A1 2000224993 A 2003148396 A1	17-10-2001 24-06-2003 08-06-2000 15-08-2000 07-08-2003

Form PCT/ISA/210 (patent family annex) (January 2004)